

Mortality of workers in a French asbestos cement factory 1940–82

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ABSTRACT The mortality of a complete cohort of 1506 French asbestos cement workers employed for at least five years is related to the time elapsed since first exposure. The mortality from all causes (analysed by the “man-years method”) has been found to be above normal only in those subjects employed for more than 20 years, with more than 35 years of follow up. Standardised mortality ratios for cancers of all sites (ICD 140–209) and pulmonary cancer (ICD 162–163.0) have been assessed in subjects whose first exposure dates go back more than 20 years. Mortalities from cancer of all sites and from pulmonary cancer have been detected in excess in workers employed for more than 20 years and originally hired when aged 25 or under.

Several epidemiological studies in the past 15 years have shown evidence of an excess mortality due to different cancers in asbestos workers: the tumours associated with exposure to asbestos include mesotheliomas,¹ bronchogenic carcinoma² for which the carcinogenic role of asbestos has been shown,^{3,4} and tumours of the gastrointestinal tract,² where there is doubt concerning the causal role of asbestos,⁵ although in some cases peritoneal mesotheliomas have been classified as cancer of the pancreas^{1,6} and, finally, cancer of the larynx² where contradictory results have been found.^{4,7}

Most of the early studies in this area were carried out on workers handling pure asbestos,^{8,9} and few have been undertaken on workers handling asbestos cement. Hughes and Weill have detected an excess of respiratory cancer mortality in workers with moderate and heavy exposure¹⁰ and Henderson and Enterline have observed a high risk of respiratory cancers in workers engaged in manufacturing asbestos cement tubes.¹¹ Lacquet and Van Der Linden showed evidence of excess mortality only from gastrointestinal cancer¹² whereas Finkelstein has observed an excess mortality from all causes and a high excess of mortality from cancer of all sites (relative risk γ 5) as well as from lung cancer (relative risk γ 8).¹³

The fact that we were able to provide further data on this subject, despite the anonymity of death certificates that, in France, limits such studies, led us

to investigate the mortality of workers at an asbestos cement factory.

Materials and methods

Our study consists of assessing the risk of mortality from all causes in a cohort of asbestos cement workers and of the risk of mortality from cancer of all sites (ICD 140–209) and pulmonary cancer—that is, lung and pleural cancers: ICD 162–163.0—in those subjects whose elapsed time since first exposure is greater than 20 years, “in order to maximise the possibility of detecting carcinogenic risk.”¹⁰

The factory is at Paray-Le-Monial in the centre of France. It was founded in 1940 and manufactures corrugated or flat plates, tubes, and various moulded objects, using mainly chrysotile asbestos except for tubes where a mixture of chrysotile and crocidolite is used.

Since January 1940, the few women (4%) employed have always worked as members of the administrative staff. The factory population, which is geographically stable, has included a few migrant workers (9%) who, with the women, have been excluded from the study. As employees with a short duration of employment (specially those first employed many years ago) would have been particularly difficult to trace, the workers selected for the study were those who had been employed for at least five years. The total cohort numbers 1506.

Each worker was followed up from the date of his first employment in the factory (taken as his first

Table 1 *Description of the cohort by age group*

Age	No of subjects		Man-years of observation as a function of time elapsed since first exposure	
	At start of exposure	At end of observation	≤20	>20
10-14	130		86.00	
15-19	386		1743.50	
20-24	357		3430.50	
25-29	185	3	4801.50	
30-34	139	173	4932.25	63.75
35-39	112	211	3877.75	668.75
40-44	81	185	2965.75	1169.75
45-49	58	227	1976.25	1368.50
50-54	32	214	1473.75	1040.00
55-59	22	152	986.75	759.00
60-64	4	119	602.50	516.50
65-69		67	322.25	373.75
70-74		55	123.50	246.50
75-79		31	19.75	131.75
80-84		11	0.75	60.75
>85		8		22.75

Table 2 *Description of the cohort by time elapsed since first exposure*

Time elapsed since 1st exposure	No of subjects contributing for calculation of man-years*	Man-years of observation	No of deaths
≤20	1506	27342.75	99
>20 ≤25	941	3581.75	49
>25 ≤30	542	1799.50	29
>30 ≤35	242	801.75	19
>35	118	238.75	10

*Each subject observed for more than 20 years (at least 20.25 years) contributes 20 man-years to the class of time elapsed since first exposure less than or equal to 20 years and for the rest of his period of observation to the succeeding five year classes.

exposure to asbestos) up to his death or to the end of the follow up period (31 December 1982) whichever occurred soonest.

Date of birth, dates of beginning and end of employment and date of death (during employment or after retirement) were obtained from the staff register kept up to date for administrative purposes since the foundation of the factory. The eventual date of death for those workers who left the factory before retirement (and therefore were not followed up in the staff register) was obtained by contacting the relatives whenever possible, otherwise by obtaining the information directly from the local registry

office. Causes of death were obtained from hospitals and family doctors.

The method used to estimate the mortality risk was "the man-years method"¹⁴⁻¹⁶ which allows a comparison to be made between the mortality of a defined group of subjects with the expected mortality that would have occurred had the group experienced the same death rate as that of a standard population, in this case the French male population.

The different dates necessary for calculating the age-time-specific man-years (dates of birth, entry and exit of observation) are expressed in completed quarterly years (January 1940 = 1940.00, April 1940 = 1940.25); then, man-years are computed in years and quarterly years. Table 1 shows the distribution of the cohort within age-classes and the corresponding man-years and table 2 shows the distribution according to time elapsed since first exposure.

Cancer mortality was analysed in those whose elapsed time since first exposure is over 20 years. For this analysis the cohort (a total of 941) has been subdivided according to the duration of employment: between five and 20 years (357 subjects) and more than 20 years (584) (table 3).

The "expected deaths" (based on the age specific death rates for the French male population¹⁷⁻¹⁹) are

Table 3 *Description of the cohort by duration of employment more than 20 years after first exposure*

Time elapsed since 1st exposure (years)	Duration of employment (years)					
	5-20			>20		
	No of subjects contributing to calculation of man-years	Man-years of observation	No of deaths	No of subjects contributing to calculation of man-years	Man-years of observation	No of deaths
>20 ≤25	357	1327.00	28	584	2254.75	21
>25 ≤30	196	645.50	13	346	1154.00	16
>30 ≤35	88	291.50	9	154	510.25	10
>35	42	91.75	1	76	147.00	9

calculated by five year age classes and by five year periods beginning 1 January 1940 for mortality from all causes and beginning 1 January 1960 for mortality from cancer.

The mortality risk is expressed by the standardized mortality ratio (SMR). The significance of the SMR was tested by assuming that, under the null hypothesis, the number of observed deaths originated from a Poisson distribution with mean equal to the number of expected deaths.¹⁶

Table 4 *Distribution of causes of death by time elapsed since first exposure and by duration of employment more than 20 years after first exposure*

Cause	Period since first exposure (years)		
	≤20	>20	
		Duration of employment (years)	
		5-20	>20
All causes	99	51	56
Cancer all sites:	18	12	23
Peritoneal mesothelioma	1	0	0
Pleural mesothelioma	0	0	3
Lung	3	3	6
Digestive system	6	3	5
Otorhinolaryngology	3	3	4
Other	5	3	5
Non-malignant pulmonary disease	6	3	0
Cardiovascular disease	22	17	13
Digestive disease	1	0	2
Alcoholic cirrhosis	9	4	12
Suicide	8	2	2
Accident	15	0	3
Other	3	4	0
Unknown cause	17	9	1

Table 5 *SMR from all causes in function of time elapsed since first exposure*

Time elapsed since first exposure (years)	O/E*	SMR
≤20	99/128.04	0.77†
>20 ≤25	49/39.74	1.23
>25 ≤30	29/29.98	0.97
>30 ≤35	19/20.26	0.94
>35	10/6.62	1.51
Total >20	107/96.60	1.11

*Ratio of observed to expected deaths.

†p < 0.01.

Table 6 *SMR all causes, within employment duration more than 20 years after first exposure*

Time since 1st exposure (years)	Employment duration (years)			
	5-20		>20	
	O/E	SMR	O/E	SMR
>20 ≤25	28/22.19	1.26	21/17.56	1.20
>25 ≤30	13/15.77	0.82	16/14.21	1.13
>30 ≤35	9/10.10	0.89	10/10.16	0.98
>35	1/2.75	0.36	9/3.87	2.33*
Total >20	51/50.81	1.00	56/45.80	1.22

*p < 0.05 (assuming a Poisson distribution).

Results

We had no loss to follow up and 206 deaths occurred in the cohort during the study period. Of those, it was possible to identify the cause of death for 179 subjects (87%). The causes of death are listed in table 4 according to the time elapsed since first exposure and, for those that occurred more than 20 years after first exposure, according to duration of employment.

OVERALL MORTALITY

Table 5 shows the observed and expected number of deaths and the SMRs. In subjects from whom the time since first exposure does not exceed 20 years a SMR value of 0.77, significantly less than 1, was observed. There was no significant excess mortality in the subcohorts with an observation duration exceeding 20 years when the duration of employment was not taken into account. When it was, however, it may be seen (table 6) that in workers with less than 20 years' employment the SMRs are not significantly different from 1 and the overall SMR value is 1.00, whereas in workers with more than 20 years' employment the overall SMR value is 1.22. The highest SMR (SMR = 2.33, significantly greater than 1) was found in workers whose time since first exposure was the longest.

CANCER MORTALITY

The deaths from mesothelioma and from lung cancer are detailed in table 7. The four deaths from mesothelioma were one from peritoneal mesothelioma occurring less than 20 years after first exposure and three from pleural mesothelioma occurring more than 20 years after first exposure. The average latent period is close to 25 years. As regards lung cancer, three deaths occurred less than 20 years after first exposure, with an average latency of 13 years and nine occurred more than 20 years after the first exposure, with an average latency of 25½ years. The mortality rates for lung cancer and mesothelioma were estimated by age group and the results are shown in table 8. For lung cancer, the

highest death rate was in those aged 65 and over; for mesothelioma, it was in the 45–54 age group.

Considering only subjects who have been followed up for more than 20 years since first exposure (table 9), no excess mortality occurs in those with the shortest duration of employment (5–20 years). For those with more than 20 years of employment, a significant excess mortality from cancer of all sites (SMR = 1.68) was noted; there was no excess of death from causes other than cancer (SMR = 1.03).

The SMR for pulmonary cancer in the workers with the longest duration of employment (SMR = 2.99) is significantly greater than 1, whereas the SMR for other cancers is not.

As people with the longest employment were hired younger than those with the shortest employment (average ages 28.4 and 41.1 respectively for those whose period of employment over 20 years and between five and 20 years), we calculated SMRs according to age at first exposure for each level of

Table 7 Description of mortality by mesothelioma and lung cancer in function of time elapsed since first exposure

Causes	Time elapsed since first exposure (years)	
	≤20	>20
Mesothelioma:		
No	1*	3†
Average age at onset of exposure	28	21.8 (range = 16.3–26.0)
Average age at death	41.5	46.5 (range = 41.8–52.5)
Latency period	13.5	24.8 (range = 22.3–26.5)
Lung cancer (ICD: 162):		
No	3	9
Average age at onset of exposure	37.3 (range = 18–49.5)	30.3 (range = 18.5–43)
Average age at death	50.6 (range = 37–64)	56.0 (range = 46.8–71.3)
Latency period	13.3 (range = 6.3–19)	25.7 (range = 21.3–30.5)

*Peritoneal mesothelioma.

†Pleural mesothelioma.

Table 8 Lung cancer and mesothelioma death rates by age group, in function of time elapsed since first exposure

Cause Time elapsed since 1st exposure (years)	Age				Total
	35–44	45–54	55–64	≥65	
Lung cancer:					
≤20					
No	1	1	1	0	3
Rate‡	0.15	0.30	0.63	—	0.24
>20					
No	0	5	2	2	9
Rate‡	—	2.08	1.57	2.39	1.42
1970 rate‡	0.09	0.36	1.25	2.11	
Mesothelioma:					
≤20					
No	1†	0	0	0	1
Rate‡	0.15	—	—	—	0.08
>20					
No	1*	2*	0	0	3
Rate‡	0.54	0.83	—	—	0.47

*Pleural mesothelioma.

†Peritoneal mesothelioma.

‡Rates for 1000 person-years.

Table 9 SMR from causes within employment categories more than 20 years after first exposure

Cause	Employment duration (years)					
	5-20		>20		Total	
	O/E	SMR	O/E	SMR	O/E	SMR
Cancers all sites (ICD 140-209)	12/12.82	0.94	23/13.72	1.68*	35/26.54	1.32
Causes other than cancers	39/37.99	1.03	33/32.08	1.03	72/0.07	1.03
Pulmonary cancers (ICD 162-163.0)	3/2.51	1.20	9/3.01	2.99†	12/5.52	2.17*
Cancers other than pulmonary	9/10.01	0.87	14/10.71	1.30	23/21.02	1.09

*p < 0.05.

†p < 0.01.

Table 10 SMR from cancers (all sites and pulmonary) in function of employment and age at first exposure

Cause	Age at 1st exposure	Employment duration (years)					
		5–20		>20		Total	
		O/E	SMR	O/E	SMR	O/E	SMR
Cancers all sites (140–209)	≤25	5/1-99	2-51	10/3-68	2-72*	15/5-67	2-67†
	>25	7/10-83	0-65	13/10-04	1-29	20/20-87	0-96
Pulmonary cancers (162–163-0)	≤25	1/0-41	2-43	4/0-77	5-19*	5/1-18	4-23*
	>25	2/2-10	0-93	5/2-24	2-23	7/4-34	1-61

*p < 0-01.

†p < 0-001.

duration of employment. The results (table 10) show that the SMRs are also higher in people hired before the age of 25. The greatest value (SMR = 5-19) was obtained for pulmonary cancer in those who were first hired before the age of 25 and employed for more than 20 years.

Discussion

GENERAL MORTALITY

The SMR (0-77) for those whose duration of exposure is less than or equal to 20 years illustrates the phenomenon of the healthy worker effect; a similar result was found by Selikoff *et al* in insulation workers.² Among subjects whose time since first exposure is greater than 20 years the risk is greater in those with the longest time since first exposure. The SMR for the entire cohort followed up for more than 20 years since first exposure (1-11) is lower than that obtained by Selikoff *et al* in insulation workers (SMR = 1-41)² or that estimated by Finkelstein in asbestos cement workers (SMR = 2-0)¹³; it is close to that evaluated from the results of McDonald *et al* in chrysotile mine workers in Quebec (SMR approximately 1-1 for the categories of "gross service" over five years)⁴; it is much higher than that estimated from the results of Hughes and Weill in asbestos cement workers, approximately 0-7, but in that study about 60% of workers had been employed for less than one year.¹⁰

CANCER MORTALITY

The results presented here are limited by the quality of the information on the causes of death. For the complete cohort, the total number of non-identified causes is greater in the subjects whose employment was less than 20 years (26 of the 27 non-identified deaths) and, among them, in those who began to work a long time ago (23 non-identified deaths occurred in subjects having entered the factory before 1960 and stayed less than 20 years). Among those with more than 20 years since first exposure it is in the group with short duration of employment that most of the non-identified causes of death

occurred (9/1). With regard to the quality of the information, the physician who collected the data was in a privileged position to obtain first hand information. The son of the medical practitioner in Digoin, he was himself a practitioner in Paray-le-Monial for 25 years. The factory is between these two towns, which are within seven miles of each other. This was a considerable advantage when contacting the families, hospital and regional doctors, and neighbouring town halls. As mentioned before the French method of registering deaths does not provide the cause of individual deaths. Nevertheless, had we obtained the death certificates, the non-identified causes would have been 9% in the 35–39 year age group to 16% in the 85–89 year age group²⁰ instead of the 9% in those of our subjects observed for more than 20 years—that is, in the subjects studied for mortality from cancer at all sites and pulmonary cancer.

For cancers at all sites, in the subjects with more than 20 years' employment, our SMR of 1-68 (significantly greater than 1) is higher than that obtained by McDonald *et al* in chrysotile mine workers (SMR y 1-2 for "gross service" greater than 20 years).⁴ The SMR for our entire cohort 20 years after first exposure (SMR = 1-32), however, is less than half that found by Selikoff *et al* in insulation workers (SMR = 3-05),² and more than three times lower than that estimated by Finkelstein in asbestos cement workers in Ontario (SMR = 4-6).¹³ The deaths of unknown cause could not affect our results for cancer at all sites when one considers that, for the group of subjects observed for more than 20 years, only 10 causes were not characterised. In the most pessimistic hypothesis, which would consider that all unknown deaths were from cancers, there would be nine supplementary cancers in the class with the shortest duration of employment, and one in the other, which would result in SMR values of 1-64 and 1-75 respectively; taking the mean hypothesis, which would consider that the same proportion of cancers at all sites exists among the identified and non-identified causes, then the SMR values for those with the shortest duration of emp-

loyment would be 1.14 and 1.71 for those with the longest employment. The SMR estimated for pulmonary cancer in people whose elapsed time since first exposure is greater than 20 years ($SMR = 2.17$, significantly greater than 1) is nearly four times lower than the one assessed by Finkelstein for lung cancer alone (ICD 162)—but this latter study was made with a small number of subjects.¹³ On the other hand, it is higher than that estimated by Hughes and Weill in people whose duration of employment exceeded two years (assessed risk close to 1.5).¹⁰ The risk that we have estimated in people employed more than 20 years ($SMR = 2.99$) is significantly greater than 1, which is higher than the SMR found by McDonald *et al* in chrysotile miners with “gross service” of more than or equal to 20 years ($SMR = 1.61$)⁴ and close to that evaluated by Henderson and Enterline ($SMR = 2.70$) for retired people whose average duration of employment was 25 years.¹¹ The excess mortality from cancer at all sites found in the present study may be explained by the excess mortality observed for respiratory cancer since for cancers other than respiratory, there is no compensatory decrease in mortality.

In all cases for the same duration of employment SMRs are higher in those whose age at first exposure does not exceed 25. We may quote Peto *et al*, “lifelong regular exposure of humans to a carcinogenic insult will be more dangerous the younger exposure starts.”²⁰ We may assume that asbestos is never entirely eliminated from the organism.

Despite the eventual underestimate, due to the existence of 10 non-determined causes of death, it is interesting to note that the lung cancer mortality rates calculated for our cohort, in subjects observed from more than 20 years in the age groups 45–54, 55–64, and 65 and more, are higher than those in the French male population for the year 1970 with the greatest difference (nearly six times as great) being found in those aged 45–54 (table 8).

A remark must be made in the case of the mesotheliomas: we have observed four deaths (a proportional mortality of 2%) for which the latent period is not very long: less than 14 years for the death from peritoneal mesothelioma and an average of less than 25 years from the three deaths from pleural mesothelioma. Selikoff *et al* observed 175 cases of mesothelioma in 2271 deaths (8%) and the highest incidence appeared about 40 years after the onset of exposure.²¹ So possibly in our case the average time elapsed since first exposure is not long enough—a mean of 22.4 years, with only 118 men observed for more than 35 years since the onset of exposure to appreciate the full impact of the exposure²¹ and that what we observe here are the early deaths from mesothelioma. The latent period for

pleural tumours, however, is greater than that observed by Hughes and Weill who suggested that “the latent period for the development of asbestos related malignant disease may be less than 20 years.”¹⁰ With the exception of one of these subjects who died from pleural mesothelioma, all were in contact with crocidolite dust during the whole duration of their employment. The number of deaths by mesothelioma could have been underestimated because 27 causes of death were unidentified. It seems unlikely, however, that we could not have been warned of deaths from this cause during our inquiry, because the respondents, all located within the region containing the factory, were very aware of the risks of mesothelioma.

In conclusion, our work has shown an excess mortality from cancer of all sites in subjects whose duration of employment exceeded 20 years and who were hired before the age of 25. This excess may be explained by an excess of deaths from pulmonary cancer (lung and pleura). We have no evidence for an excess of deaths from cancer in subjects who have worked less than 20 years, but in this group deaths from cancer may have been underestimated.

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